

REMARKS

Following entry of this amendment, claims 1-7 and 12-24 will be pending in this application. Claim 7 is currently amended, and new claims 15-24 are added. Support for the amendments and new claims can be found throughout the specification and claims as filed, e.g., at paragraphs [0035], [0036], [0080], [0081]. No new matter has been added.

35 U.S.C. § 103

Claims 1-7 and 12-14 were rejected as allegedly unpatentable over WO 00/38730 in view of Geiger et al., 2001, Cancer Res., 61:8513-19 (“Geiger”) and Kaliński et al., 1998, J. Immunol., 161:2804-09 (“Kaliński”), as evidenced by a material safety data sheet for NS-398 (“MSDS”). Applicants respectfully traverse the rejection.

At pages 5-6, the Office Action states:

[I]t would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a dendritic cell as the vaccine, as taught by Geiger et al., in the method of treating cancer of WO 00/38730. The ordinary artisan at the time the invention was made would have been motivated to do so and have a reasonable expectation of success, since Geiger et al. teach that dendritic cells can be used as a vaccine for treating cancer. Furthermore, WO 00/3870 teaches that inhibition of COX-2 decreases PGE-2 production, and Kalinski et al. teach that PGE-2 inhibits IL-12 production and TH1 priming by dendritic cells. Thus, the ordinary artisan would be motivated to administer a combination of a COX-2 inhibitor with a dendritic cell vaccine to inhibit PGE-2 production in order to enhance IL-12 production and Th1 priming by the dendritic cells in vivo.

The Office has cited WO 00/38730 as allegedly disclosing “a method of treating cancer in a human subject comprising administering a combination of a COX-2 inhibitor and a vaccine to the subject” (page 3). At the same page, the Office Action admits that “WO 00/38730 does not teach administering a dendritic cell as the vaccine component.” Applicants note that the disclosure of WO 00/38730 with regard to vaccines is particularly limited. The term “vaccine” appears only three times in the entire document. Further, WO 00/38730 does not teach or suggest that inhibition of COX-2 would be useful to enhance the effectiveness of a vaccine, much less a dendritic cell vaccine.

The Office has cited Geiger as allegedly disclosing “that dendritic cells can be used as a vaccine to induce an immune response and treat cancer in human patients” (page 3). As noted by the Office, Geiger discloses the use of “immature dendritic cells that have been pulsed with tumor lysate *in vitro*” (page 3). Geiger does not teach or suggest the administration of mature dendritic cells, as recited in claims 15-24. Further, applicants disagree with the Office’s interpretation of “unprimed” dendritic cells to encompass “immature dendritic cells which have not been treated or primed *in vitro* with maturation factors” (page 4). Such an interpretation is not supported by Geiger or the specification. Geiger uses the term “priming” only in relation to T cells, not with respect to dendritic cells (see abstract). Although the specification does not provide explicit definitions of the terms “primed” and “unprimed”, applicants submit that the specification makes clear that primed dendritic cells are those that have been exposed to antigens and that have, e.g., acquired, processed, and/or been loaded with the antigens, whereas unprimed dendritic cells are those that have not acquired, processed, and/or been loaded with antigens. See, e.g., paragraphs [0044] and [0045] of the specification. As all of the dendritic cells used in Geiger had been pulsed with tumor cell lysates, Geiger does not teach or suggest the administration of unprimed dendritic cells.

The Office action alleges that Kaliński discloses that “PGE-2 impairs IL-12 production and Th1 priming capacity of dendritic cells if it is present when dendritic cells are undergoing maturation” (page 4). Applicants note initially that Kaliński is directed to investigating mechanisms of dendritic cell maturation *in vivo*. Accordingly, Kaliński does not teach or suggest the administration of dendritic cells to treat cancers or the use of COX-2 inhibitors in combination with already mature dendritic cells, as recited in claims 15-24. Further, Kaliński does not teach or suggest the use of dendritic cells that have been primed with antigens, e.g., tumor antigens.

Applicants submit that a *prima facie* case of obviousness has not been made. None of the cited references, alone or in combination, teaches or suggests treatment of cancers with dendritic cells in combination with COX-2 inhibitors.

Additionally, none of the references teaches or suggests administration of mature dendritic cells, as recited in new claims 15-24, or administration of unprimed dendritic cells, as recited in claims 13 and 23.

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CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is requested. This response is being submitted with a Request for Continued Examination, a Petition for Extension of Time, and the required fees. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 22862-0003US1.

Respectfully submitted,

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